BEDSIDE MEDICINE FOR BEDSIDE DOCTORS

An Open Forum for brief discussions of the workaday problems of the bedside doctor. Suggestions of subjects for discussions invited.

PREANESTHETIC DRUGS

I. A PHARMACOLOGIST'S VIEWPOINT*

C. D. LEAKE, Ph.D. (University of California Medical School, San Francisco).—Proper psychic preparation of a surgical patient, by an anesthetist who appreciates something of the psychology of fear and of the means by which the dread of a surgical operation may be minimized, will do much to improve such a patient's general status before the actual anesthetic is administered. But for the average patient, where time is not always available for this procedure, a suitable preanesthetic hypnotic may be necessary to supplement the anesthetist's psychic approach. A preanesthetic hypnotic, however, is not indicated solely for the relief of fear the patient may have for anesthesia; it has a definite function in the actual induction and conduct of the anesthesia. As pointed out so strikingly by Waters and Guedel,[1] such an hypnotic is most useful in lowering the patient's general metabolic level to a point where the anesthetic may be easily and smoothly administered.

Preanesthetic hypnosis certainly reduces the amount of anesthetic agent required, so that during the direct anesthesia more oxygen may be given than would otherwise be the case, were no preliminary depressant agent employed. Thus, with proper preanesthetic preparation, a satisfactory degree of surgical anesthesia may be readily secured even by nitrous oxid and oxygen without pushing nitrous oxid to a dangerous asphyxial concentration, which is frequently necessary without supplementary depression.

Although much general dissatisfaction has been expressed with morphin and hyoscin (scopolamin) as *preanesthetic hypnotics,* they continue to be used quite routinely in the absence of any pressing clinical necessity for something better. Morphin is definitely indicated, of course, as a *preanesthetic analgesic* when pain is present. A consideration of the pharmacology of these agents may be of interest in supporting the independent clinical condemnation of these agents for *preanesthetic hypnosis* years ago by such competent observers as Herb, Gatch, and Bevan.[2]

The primary effect of morphin is stimulation of the central nervous system, which is promptly masked in humans by a secondary depression. *The stimulating action outlasts the depression.* Thus, after the depression wears off there is increased irritability and cortical excitement, which may be responsible for the initiation of craving and habit. That is, during the after-period of irritability the individual craves the drug again in order to recover the pleasant euphoria of the depressant stage.[3] Another objection to morphin as an adjunct to anesthesia is its tendency to cause constipation, which interferes with a proper postanesthetic condition. However, the definite stimulation of intestinal musculature by morphin may help greatly in preventing postoperative intestinal stasis.[4] Furthermore, morphin is not helpful in anesthesia because its action in depressing respiration interferes with the rapidity of absorption or elimination of an inhalation anesthetic. To these three important pharmacologic objections might be added its tendency to disturb carbohydrate metabolism, in a manner not conducive to the best condition of the patient, as reflected in its effect on blood sugar and on the acid-base balance of the blood.[5] In justice to morphin, however, it should be noted that the clinical opinion, that it interferes with kidney function, has little support when critically examined.[6] The suppression of renal activity under anesthesia seems to be a reflex effect of irritation of the laryngeal mucous membrane by the anesthetic gases.[7]

There is no doubt, however, that morphin remains the best preanesthetic hypnotic when *traumatic* pain is present. Its amazingly effective action in relieving traumatic pain should not be denied the patient, either before or after the operation, if its use is indicated. The National Research Council is spending a great sum of money annually to finance chemical research at the University of Virginia, and pharmacologic work at the University of Michigan under the direction of Dr. N. B. Eddy, to develop a satisfactory substitute for morphin which will be free from its addiction dangers. The resultant pharmacologic studies are currently appearing in the *Journal of Pharmacology and Experimental Therapeutics.* Meanwhile, a morphin derivative called "dilaudid" was enthusiastically introduced in this country by Alvarez.[8] Subsequent clinical use has indicated, however, that "dilaudid" has probably the same potential addiction properties as those possessed by morphin. Dr. Norman A. David, formerly of this laboratory, has made an interesting comparison of the two agents.[9]

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* From the Pharmacological Laboratory of the University of California Medical School, San Francisco.

1 Waters, R. A., and Guedel, A. E.: Personal communication.

2 Herb, I. C.: J. A. M. A., 56:1312, 1911. Gatch, W. D.: *Ibid.,* 57:1599, 1911. Bevan, A. D.: *Ibid.,* 57:1821, 1911.

3 Collins, K. H., and Tatum, A. L.: J. Pharmacol. and Exper. Therap., 27:237, 1926.

4 Plant, O. H., and Miller, G. H.: J. Pharmacol. and Exper. Therap., 21:202, 1923.

5 Leake, C. D., and Koehler, A. E.: Arch. Internat. de pharmacodyn. et de thérap., 27:221, 1922.

6 Haines, W. H., and Milliken, L. F.: J. A. M. A., 85:1853, 1925.

7 Dooly, M. S., and Wells, C. J.: Am. J. Physiol., 90:330, 1929.

8 Alvarez, W. C.: Proc. Staff Meet., Mayo Clinic, 7:480, 1932.

9 David, N. A.: J. A. M. A., 103:474 (Aug. 18), 1934.

Little rational evidence exists that opium or a mixture of its alkaloids free from non-alkaloidal material ("pantopon") has any advantage over morphin as a preanesthetic hypnotic. Such a mixture of the differently acting alkaloids in opium is an irrational material to use, since not only aggravation of some of the deleterious effects of morphin, as its constipating action, is known to occur by giving it with other opium alkaloids, but indeed few of these other alkaloids have been properly studied, either pharmacologically or clinically, to know how they may act. Scientific therapy demands the use of chemical agents singly for definite effects, avoiding confusing mixtures of any sort. Certainly, preanesthetic hypnosis should be simplified and rationalized rather than complicated.

If there is pain present due to swelling of tissue, then morphin is not as effective as such drugs as amidopyrin, the salicylates or the cinchophens. These antipyretics exert their pain-relieving action, when pain is due to swelling of tissue, by pulling fluids out of such swollen tissue back into the blood stream, as indicated by the careful studies of Barbour.[10]

Hyoscin or scopolamin is said to synergize with morphin, enhancing its depressant action, especially on the cortex. The pharmacology of hyoscin has not been very thoroughly studied, and there seem to be few clinical observations of a critical nature on the effects of this drug in connection with anesthesia. Hyoscin is chemically related to atropin and has a similar effect on the autonomic nervous system. This action, as we shall see, may be detrimental in preanesthetic medication. In the absence of any reliable or critical evidence of its usefulness as a preanesthetic hypnotic, little justification exists for its continued use merely because of clinical habit or routine. There is an opportunity here for clinical judgment to evaluate critically its status as an adjunct to anesthesia. Barlow has recently shown experimentally that hyoscin is of no value in nitrous oxid anesthesia and, indeed, it may be detrimental.[11]

In the effort to find more satisfactory preanesthetic hypnotics which might be substituted for morphin, a number of other substances were studied in my laboratory from the point of view of their effects on the body functions of normal human subjects, in comparison with morphin.[12] We studied especially the action of these various depressant drugs on basal metabolic rate, tactile discrimination, respiration, pulse rate, and blood pressure. We thought our observation might furnish us with objective quantitative criteria for estimating depressant action of the different drugs on the central nervous system. While codein has much to recommend it over morphin as a central nervous system depressant, it is not sufficiently powerful, in our judgment, to justify its use clinically for preanesthetic hypnosis.[13]

The exploitation of sodium amytal suggested that we study barbital and its common derivatives from this standpoint. *As a result of our observations on normal humans, we may recommend barbital by mouth as a possible substitute for morphin as a preanesthetic hypnotic, if no pain is present.* In the average adult it may be expected to bring relief from fear and apprehension, and to dispose toward sleep, relaxation and amnesia, in doses of 1 to 1.5 grams, or even higher. It depresses the basal metabolic rate in the same way as morphin, and is otherwise generally depressing. No residual stimulation results, and the psychic disadvantage of hypodermic administration is avoided. It may sometimes cause a cutaneous rash, however, and it is of no use as a hypnotic if pain is present. Subjective reactions to barbital vary greatly with physical constitution and social background. If the ordinary local anesthetics are to be used, it is definitely indicated since it protects against their toxic manifestations.[14] With spinal anesthesia, the status of which still remains to be established, more of an analgesic effect is needed in the preanesthetic medication, and morphin or amidopyrin is indicated.

We could not find that phenobarbital, or any of the common commercial modifications of barbital, including "amytal," "dial," "ipral," "neonal," and "phanodorn," have any significant advantages over barbital as hypnotic agents in man. Indeed, they all showed some disadvantages.[15] Eddy, however, from animal experiments, believes "amytal" has the greatest depressing effect.[16]

It is sometimes amusing to the pharmacologist to observe the enthusiasm with which certain clinicians continue to report experiences with new drugs. There seem to be fads and styles with drugs as with clothes. If medical men generally realized the extent to which preliminary and unconfirmed pharmacologic evidence is distorted by drug concerns (usually foreign) for clinical exploitation of new agents, they would undoubtedly be more reserved in expressing clinical opinions. Very few new drugs reach clinical trial in an ideal scientific manner.[17]

Sodium amytal was thus overenthusiastically recommended as a general anesthetic when given in strongly alkaline solution by vein. While the induction of sleep and amnesia is dramatic by this technique, it is obvious that the agent is not in itself sufficiently analgesic to be a satisfactory general anesthetic except in dangerous doses. There is too narrow a margin of safety between the dose causing real anesthesia and that depressing the medullary centers to a lethal level. Sodium amytal thus falls in the class of anesthetic adjuncts, as now admitted by its original proponent.[18] The intravenous, or even oral, use of this

10 Barbour, H. G.: J. Pharmacol. and Exper. Therap., 29:427, 1926.

11 Barlow, O. W.: J. Pharmacol. and Exper. Therap., 46:131, 1932.

12 Anderson, H. H.: Proc. Soc. Exper. Biol. and Med., 27:102, 1929.

13 Chen, M. Y., and Anderson, H. H.: Proc. Soc. Exper. Biol. and Med., 27:719, 1930.

14 Tatum, A. L., and Collins, K. H.: Arch. Int. Med., 38:405, 1926. Knoefel, P. K., Herwick, R., and Loevenhart, A. S.: J. Pharmacol. and Exper. Therap., 39:397, 1930.

15 Leake, C. D., Chen, M. Y., and Anderson, H. H.: J. Pharmacol. and Exper. Therap., 40:215, 1930.

16 Eddy, N. B.: J. Pharmacol. and Exper. Therap., 33:43, 1928.

17 Leake, C. D.: J. A. M. A., 93:1632 (Nov. 23), 1929.

18 Zerfas, L. G., and McCallum, J. T.: Anesth. and Analg., 8:349, 1929.

substance as a routine preanesthetic hypnotic is not justified until it has been more thoroughly evaluated in comparison with what, in our opinion, is as satisfactory, and certainly a less expensive official drug, barbital.

A new German barbital derivative, called "evipal," has recently been exploited for intravenous anesthesia. It is subject to the same general criticisms as sodium amytal by vein. It has, however, one advantage in that it seems to be fairly rapidly destroyed in the body, so that recovery from an anesthetic dose is, consequently, rapid.

Stormount[19] and associates have directly studied the preanesthetic value of various barbitals in nitrous oxid and oxygen anesthesia in rats. They found that 85 per cent nitrous oxid with 15 per cent oxygen (enough to prevent anoxemia at sea level) will anesthetize with 30 per cent of the average lethal dose of "dial" and "neonal," but that 45 per cent of the average lethal dose of "amytal," barbital, and phenobarbital is required to give this same effect. In man, however, we found barbital the most satisfactory depressant of the series, in so far as lowering of the basal metabolic rate, dulling of tactile discrimination, and tending toward sleep are concerned. Amytal and phenobarbital, we noted, increased the basal metabolic rate except in high doses. The relative merits of the several derivatives of barbital as preanesthetic hypnotics remain, therefore, to be further evaluated before surgeons are justified in using any of its modifications for this purpose, in preference to the well-studied parent substance, barbital.

It is hardly possible that any of the other multitudinous commercial derivatives of urea exploited so vigorously, especially by the Germans, have any great advantage over barbital in this regard. One of these, "pernocton,"[20] includes bromin, which introduces another difficult depressant factor to evaluate. Chemists have sought for some time to develop barbital derivatives which are rapidly destroyed or removed from the body. One of these, "evipal," has already been mentioned. In this country the Lilly and Abbott laboratories developed, almost simultaneously, an identical compound called, by the former, "pentobarbital," and by the latter, "nembutal." These barbitals are relatively short in action, but the effects of repeated administrations must still be carefully studied in order to determine whether any residuum remains which may lead to the danger of chronic poisoning.

Particularly to be condemned are combinations of barbital or its derivatives in fixed proportions with amidopyrin, such as "allonal," "cibalgin," or "pyraminal." Aside from the violation of rational therapy by such mixtures of a hypnotic with an analgesic in fixed proportions without regard to the indications of the individual patient, as scored by the Council on Pharmacy and Chemistry,[21] Koppanyi and Lieberson[22] have shown that the analgesic component of such mixtures is eliminated much more rapidly than the hypnotic, so that grave danger of the cumulative effect of the latter is present if the dose is repeated to get continued analgesic action.

The same general considerations hold for tribrom-ethyl alcohol ("avertin"). Enthusiastically advocated as a general anesthetic by those who hitherto rarely saw good modern anesthesia by gas and oxygen, more critical clinical opinion now recognizes this agent more properly as merely an adjunct to anesthesia.[23] The difficulties of preparation, the dangers of toxic decomposition, the necessary mode of administration and the pharmacologic action of the drug limit its usefulness, as in the case of sodium amytal by vein, to abnormally apprehensive or excited patients, and then in doses not so high as to give partial analgesia with dangerous depression of the vital centers—that is, not much more than 75 milligrams per kilo body weight. It is peculiar that physicians should become so excited over tribrom-ethanol by rectum, when paraldehyd, a much cheaper and safer drug, was used in this manner as a preanesthetic agent many years ago. The enthusiasm over tribrom-ethanol has revived interest in paraldehyd as a safe and effective preanesthetic hypnotic.[24]

The prolonged action of tribrom-ethanol and of the barbitals, especially sodium amytal by vein, may have a useful postoperative effect in keeping the patient quiet and asleep. But often with the barbitals motor excitement may supervene, especially if large doses are used, and contrariwise, if the dose is too high, such severe depression may result that constant attention is needed to prevent accidental asphyxiation or other complications.

The central nervous system depressant action of magnesium sulphate and its dramatic antagonism by calcium chlorid were demonstrated experimentally by Meltzer and Auer[25] in 1908. Clinically developed by Gwathmey[26] for aid in preanesthetic hypnosis, its possible field of service has become somewhat neglected in the undignified rush to help exploit the newer commercialized drugs. The characteristic feature of its action is depression of motor tone and activity, so that it would seem to be especially indicated in patients with motor excitement or with so much muscular tone as to interfere with satisfactory surgery. One or two cubic centimeters of a 50 per cent sterile solution injected intramuscularly is an average dose for this effect. It is claimed that the drug synergizes with morphin and the general anesthetics, so that care must be observed in its use with these agents.

Atropin was introduced as an adjunct to chloroform anesthesia, in order, by paralyzing the pe-

19 Stormount, M. F., et al.: J. Pharmacol. and Exper. Therap., 39:165, 1930.

20 Raeschke, J.: Klin. Wchnschr., 8:1800, 1929.

21 Council on Pharmacy and Chemistry: J. A. M. A., 86:1853 (June 12), 1926.

22 Koppanyi, T., and Lieberson, A.: J. Pharmacol. and Exper. Therap., 39:177, 1930.

23 Edwards, G.: Brit. M. J., 2:713, 1929. Waters, R. M., and Muehlberger, C. W.: Arch. Surg., 21:887, 1930. Wood, D. A.: Calif. West. Med., 33:719, 1930.

24 Stewart, J. D. Brit. M. J., 2:1139, 1932.

25 Meltzer, S. J., and Auer, J.: Am. J. Physiol., 23:141, 1908.

26 Gwathmey, J. T.: J. A. M. A., 85:1482, 1925.

ripheral endings of the vagi, to prevent reflex stoppage of the heart during the induction stage. With ether anesthesia it is advocated on the basis of preventing the "mucous inundation" caused by the irritant action of ether vapor on bronchial mucous membranes, and/or suppressing salivation. With modern gas-oxygen anesthesia, especially when the excellent rebreathing technique devised by Waters is used [27] (in which every aspect tends so nicely to conserve the physiologic balance of the patient), these excuses for the use of atropin do not exist. This drug should certainly not be used routinely.

Osborne points out [28] that it is not good practice from the standpoint of physiology to interfere with the protective function of bronchial secretion, as long as satisfactory cough reflex is present to prevent the formation of mucous plugs with the danger of resultant atelectasis. The bronchial and intestinal relaxation induced by atropin cannot be considered beneficial to the postoperative condition of the patient. Atropin further tends to cause some cortical stimulation, and surely the dryness of the mouth it produces is no joy to the patient already thirsty in the usual postoperative state. Atropin, therefore, in my opinion, should be reserved for use when specially indicated, as in chloroform or extensive ether anesthesia, or when there is reason to expect an embarrassing mucous or salivary secretion during the operation.

In conclusion, routine preanesthetic medication is to be strongly condemned. So also is an undignified rush to aid the clinical exploitation of new commercial agents not yet properly evaluated pharmacologically. Each patient should be separately considered, from the standpoint of preanesthetic hypnosis, with regard to type of chemical agent to be employed and, if necessary at all, dosage and mode of administration. The clinical evaluation of new agents should be left to university or research hospitals, where critical study with proper control methods are most likely to be found.

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II. AN ANESTHETIST'S VIEWPOINT

MARY E. BOTSFORD, M. D. (807 Francisco Street, San Francisco). — The selection of the drug and estimation of dosage are of as much importance in producing and maintaining safe and efficient anesthesia as the agent employed and the method of administration. Modern medicine requires that the patient come to the operating table in the best attainable physical and psychic condition. Where formerly the choice was limited to a few hypnotics, pharmacologic progress has increased their number so that it is now possible to fill the need of the individual case.

The various forms of *opium* have not so far been superseded by any of the newer discoveries, but its action may be assisted and modified by such adjuvants as the barbiturates, tribromethanol, evipal, paraldehyd, etc. According to Hewitt, idiosyncrasy to morphin exists in only 2 per cent of cases. It is more frequent in the *barbiturate group*. With the latter it is possible, in adults at least, by giving a minimal dose the night before operation, to establish the individual reaction, and the preanesthetic dose may be prescribed accordingly. The great value of the barbiturates lies in their hypnotic effect and, if given at least an hour before operation, they prevent the frequent stage of excitement which, by accelerating cardiac and respiratory action, lengthens the period of induction and necessitates the use of a greater amount of the anesthetic agent. When followed by morphin or pantopon, a quiet induction and smooth maintenance of inhalation anesthesia are ensured.

Avertin is of value in apprehensive patients and many minor operations, as well as brain surgery, where inhalation anesthetics increase hemorrhage, may be performed under its effect without further anesthetization. The addition of atropin to the dose of morphin is a routine procedure, which is strongly to be condemned, notwithstanding the fact that a large majority of the adult patients operated in this country are premedicated with a one-sixth to one-quarter grain of morphin and 1/150 to 1/120 grain of atropin. There has not yet been discovered a better preanesthetic drug than morphin, but the addition of atropin often nullifies its benefits. Atropin is the physiologic antagonist of morphin, whose sedation—psychic, cardiac, respiratory, and secretory—is of the utmost value in producing and maintaining efficient and safe anesthesia. The purpose of atropin is said to be its action on salivary glands, and if given alone it does decrease secretion; but with any form of opium it overcomes the effect of the latter in controlling mouth secretions. Further, its stimulating effect upon respiration is a definite disadvantage, particularly in abdominal surgery; the increased diaphragmatic activity interfering with intestinal relaxation, resulting in the necessity for producing too deep anesthesia.

Ether is in itself a cardiac and respiratory stimulant. The gaseous anesthetics, nitrous oxid, ethylene, and cyclopropane have little effect on cardiac and respiratory functions, when anoxemia is not present. The only logical place for atropin is in chloroform anesthesia, where respiratory stimulation is necessary.

Scopolamin, which fell into disfavor some years ago because of deaths resulting from an impure product, is being much used in combination with morphin. Sollmann finds it sedative in all doses, while even moderate doses of atropin are excitant.

Protection of the psyche from distressing mental impressions is of even greater importance in children than in adults. Psychiatrists and psychologists have demonstrated abundantly the evils, often developing years later, of mental complexes definitely traced to early impressions caused by fear, and there is no more potent factor in its production than the dread of operation, the awe-inspiring preliminaries, and the often forcible administration of anesthetics.

[27] Waters, R. M.: Arch. Surg., in press.

[28] Osborne, W.: Lecture on Surgical Applications of Physiology, San Francisco, 1930.

The addition of the barbiturates has helped immeasurably in providing an escape from the depressing effect of fear by influencing the nervous system sufficiently, when administered preanesthetically, to produce unconsciousness, or at least indifference to the sights and sounds incident to transportation to the operating room and the induction of anesthesia. The mass of evidence available in the literature, based on research conducted by pharmacologists, anesthetists, and surgeons, has proved conclusively the value of the barbiturates.

Determination of the drug and dosage should depend not only upon the kind of operative procedure, but the age, physical and mental condition of the patient.

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III. A SURGEON'S VIEWPOINT

JOHN HOMER WOOLSEY, M. D. (Woodland Clinic, Woodland). — The use of preanesthetic drugs, in the opinion of the majority, marks great advancement in the medical science because of the additional comfort and care they afford our surgical patients. As human beings endowed with comprehending minds, we reason and thereby suffer mental as well as physical injury. To the average patient there is nothing more important than the anesthetic because of the fear of giving up control of the vital processes. Preanesthetic drugs, when properly used, eradicate fear and assist in mental and physical rest. They help prepare the patient to undergo the necessary physical effort of any surgical procedure.

Safety to the Patient

The safety of the patient is always the paramount factor. Preoperative drugs should not be so powerful as to prevent the anesthetic agent from being the controlling factor. When seen in the operating room, it is true that the effect of a massive dose of preanesthetic medication generates enthusiasm, but its complications and sequelae, when observed in the postoperative period, dampen this enthusiasm.

The desired effect of preoperative medication is to quiet the patient, to eliminate apprehension, to enable the general anesthetic agent to control the patient's respiration and final relaxation, and to assist in a prompt postanesthetic recovery. How are we to obtain these?

In the first place, standardization of preanesthetic medication is impossible. It is an individual problem. Not only body weight, but age, sex, degree of nervousness, metabolic rate, and temperature are influential factors. A patient's susceptibility must, therefore, be individually estimated. This can be done by the use of divided dose—that is, a portion the evening before and another portion preoperatively the morning of the operation. Observance of the patient's reaction to a preanesthetic drug given the previous evening will more accurately determine the amount for immediate preoperative medication.

The postanesthetic recovery of a patient should be sufficiently prompt to allow voluntary response within one hour. Prolonged depression leads to retained secretion in the respiratory system and a greater tendency to partial pulmonary collapse. Instances of the dropping back of the tongue, with obstruction of the glottis and the interference of respiration, have been reported. It is also desirable to have the patient's coöperation in remaining covered, and in the administration of parenteral fluids.

Influential Factors

Body weight is the most important influential factor in determining the dosage of the preanesthetic drug. Heavily muscled individuals, such as athletes and workmen, demand more drugs than those whose weight consists of a considerable degree of fat.

Age is of importance, since under twelve years and over sixty years, the barbituric acid derivatives do not have a uniform effect and afterward are too depressive. Also in the aged, certain forms frequently stimulate unpleasant dreams and fearful memories, and in those suffering from cerebral disease toleration of these drugs is poor.

Because of its importance, let us reiterate, much depression of the respiration in the very young, the old, and in those with cerebral disease occurs with the preanesthetic drugs, and they must be used, therefore, with caution. In children drugs by mouth are not always readily absorbed, and rectal administration is often disturbing and occasionally expelled.

Sex plays a part chiefly because of the increased musculature of the male which demands, accordingly, more or less of a drug. There is a question in regard to the advisability of preanesthetic drugs in the cesarean section, for there should be no handicap to the respiratory efforts of the baby; and although many employ a barbital or morphin and claim no disturbance, others report instances of a definite depressive effect upon the baby.

Apprehension attendant upon an operation demands more sedation. A patient who has previously experienced the effect of preanesthetic medication has a certain amount of anticipation with the second administration, and will be more resistant to the same amount of the drug.

An increased metabolic rate and fever—somewhat similar factors, for they produce a more rapid absorption and elimination of any drug—demand a greater dosage. For example, in thyrotoxicosis the average dosage will produce inebriation rather than the desired drowsiness.

Choice of Medication

It is a known fact that the preliminary hypodermic of morphin, in the dosage of .015 to .01 gram (one-quarter to one-sixth grain) is of benefit; but there can be discussion as to the merits of pantopon, dilaudid, and scopolamin.

Pantopon supposedly depresses respiration less in relation to its narcotic activity, produces vomiting less readily, has less prolonged action, and is less euphoric than morphin. It has not proved to be as uniform in action and, as Barlow states, "it is not believed to have as *tranquilizing proper-*

ties as morphin." Collins of Chicago, on the other hand, is of the opinion that pantopon is a better drug than morphin. Personally, our experience is similar to that of Barlow.

Dilaudid, which is a quite commonly used drug in place of morphin, has an equal amount of narcotic effect, is excellent for routine use in relief of pain, but does not possess the desired preoperative hypnotic action.

Scopolamin (hyoscin) has no sedative effect, but does have an amnesic or disorientation phenomenon. It is this author's experience that, in the aged, this drug has been quite disturbing because of stimulation of unpleasant dreams and fearful memories. In children and adults it has a place, for it combines, with the above-mentioned effects, a depressant to the salivary and mucous secretions. Leech of Regina, Canada, recommends its use in small doses in addition to morphin, especially for children.

Tri-brom-ethyl alcohol (avertin) has a hypnotic, rather than an anesthetic effect, and it is recommended that it should be used only as a hypnotic in the production of "basal anesthesia." When used in too large a dosage, it carries with it the danger of losing the paramount factor demanded in anesthesia—the control of the patient. The demands made in the administration of this drug are comparatively great, and the period of postoperative recovery is prolonged, requiring increased nursing care. Supplemented with local anesthesia, this drug appears today to be the choice for brain surgery. In such cases, a long operation and special nursing care are the rule; but the operation, while meticulous, is not as shocking as the average celiotomy. In its favor are its complete elimination of psychic trauma, its lack of accompanying or subsequent nausea and vomiting, and its rare pulmonary sequelae. Against its use is the great potential danger to the safety of the patient in the loss of control by the attending physician or surgeon.

The *barbituric acid* hypnotics have demanded an increasing interest during the past fifteen years. There is a unanimity of opinion that oral or rectal administration is preferable and is sufficient, provided there can be an interval of three-fourths of an hour before operation. The intravenous method has too narrow a margin of safety. There is also confusion as to the best form of this drug because of the variation of hypnotic efficiency, the rate of oxidation and the speed of elimination which these barbituric acid combinations possess.

From the data available concerning some of the forms, the following facts have been determined:

Di-ethyl barbituric acid (barbital), 25 to 30 per cent, is used, is absorbed slowly, and 70 to 75 per cent is eliminated over seven to eight days.

Phenyl-ethyl-barbituric acid or phenobarbital (luminal) 80 per cent is used, is absorbed slowly, and the 20 per cent eliminated appears as late as the tenth day.

Allyl-iso-propyl barbituric acid (allonal) 80 per cent is used, is absorbed at a moderate rate, and all is eliminated by twenty-four hours.

Sodium iso-amyl-ethyl barbituric acid (sodium amytal) no definite data is available; but in comparison with phenobarbital, it is absorbed more rapidly, and has a greater and longer hypnotic effect, lasting up to ten hours.

Sodium ethyl-methyl-butyl barbituric acid or pentobarbital sodium (nembutal) no definite data is available, but in comparison with all other barbiturates it is rapidly absorbed, has a greater hypnotic and a less-prolonged effect, which is over, on the average, of four hours.

The more rapid the absorption the greater is the hypnosis, and the more rapid the elimination the quicker the recovery. Therefore, we can, with with some scientific precision, choose the barbituric derivatives best adapted to the type of patient and operation. In order to assure the patient a restful night, preoperatively, sodium amytal or sodium pentobarbital are most universally satisfactory, since they are absorbed quite completely at a moderate rate and eliminated within eight to ten hours. For the immediate preoperative use, a rapidly absorbing form (greater hypnotic power) is advisable, and sodium pentobarbital (nembutal) is the choice. For prompt postoperative recovery a quickly eliminated form should be used, and we believe sodium pentobarbital (nembutal) gives the best results.

A most satisfactory hypnosis and prompt postoperative recovery are secured when sodium amytal is given the previous evening and, according to the patient's response, a dose of pentobarbital sodium is administered one and one-half hours before operation.

Personally, we believe the barbituric acid derivatives are the most practical and the safest drugs. For preanesthetic medication we employ sodium amytal .18 gram (grains iii) or pentobarbital sodium .09 gram (grain iss) orally the evening before operation, and pentobarbital sodium (nembutal) .09 gram (grain iss) one and one-half hours before surgery, with a hypodermic administration of morphin .01 gram (one-sixth grain) and atropin .004 (1/150 grain) one-half hour before surgery. Our experience has been similar to Barlow and his co-workers, who report that 68 per cent are drowsy and uninterested in any procedure, 24 per cent asleep, and 8 per cent inebriated and move slightly when disturbed. As previously stated, the aged do not stand barbitals well; yet, recently, pentobarbital sodium—possibly because of its relatively rapid absorption and elimination—has given us the desired effect without as much mental disturbance as with the use of other barbitals.

Conclusions

One's opinion, influenced by his experience, changes from year to year; therefore, the combined opinion of the profession on this problem is desired. It seems wise to select a combination of agents for complete elimination of psychic trauma, physical relaxation and freedom from pain, without depression of the patient's vital functions, but with control of the patient during the preanesthetic, anesthetic, and postanesthetic stages.